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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,187	09/21/2001	Karen E. Sandman	NEB -164-PUS	4950

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NEW ENGLAND BIOLABS, INC.
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EXAMINER	
CELSA, BENNETT M	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 02/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/937,187	SANDMAN ET AL.	
	Examiner	Art Unit	
	Bennett Celsa	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-58* is/are pending in the application.

4a) Of the above claim(s) *46,47 and 49-58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-45 and 48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. DETAILED ACTION

Claims 40-58 are currently pending.

Claims 46-47 and 49-58 are withdrawn from consideration as being directed to a nonelected invention.

Claims 40-45 and 48 are under consideration to the extent they read on the elected invention.

Election/Restrictions

1. The following lack of unity and election of species (mailed 6/20/03) is currently outstanding.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Gp. 1, claim(s) 1-3, drawn to: fusion protein: SeCys peptide & surface protein.

Gp. 2, claim(s) 4-5, drawn to a SeCys containing surface protein.

Gp. 3, claim(s) 15, drawn to a library of SeCys terminal randomized peptides on the surface of an amplifiable genetic particle.

Gp 4, claim(s) 19, drawn to a constrained randomized peptide library comprising one or more terminal SeCys

Gp 5, claim(s) 6-9, drawn to a recombinant method of incorporating SeCys on the surface of a genetic particle..

Gp. 6, claim(s) 10-14, drawn to a method of derivatizing SeCys in SeCys containing peptides attached to surface genetic particles..

Gp. 7, claim(s) 16, drawn to a method for selecting novel ligands .

Gp. 8, claim(s) 17, drawn to a method for selecting predetermined enzyme activity.

Gp. 9, claim(s) 18, drawn to a method of identifying required DNA sequence elements for incorporating SeCys into peptides.

Gp. 10, claim(s) 20, drawn to: method for discovery of structurally constrained target ligands.

Election of Species (groups 1-10)

This application contains claims directed to the following patentably distinct species of the claimed invention:

I. A species of "amplifiable genetic particle" (Groups 1-6 and 8-10: e.g. see claims 2,5).

2. A species of "chemical derivitization of SeCys" (Groups 6 and 7: e.g. see claims 11-14).

Response to Restriction/Election

2. Applicant's election of Group I (claims 1-3: fusion protein between selenocystein peptide and "surface protein of an amplifiable genetic particle") in the reply filed on 3/23/04 and confirmed in applicant's supplemental response on 7/9/04 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Applicant's (e.g. Harriet Strumpel) further 1/11/05 telephonic election with traverse of phage as the species of "amplifiable particle" is also acknowledged. The elected invention corresponds to new claims 40-45 and 48. It is noted that Product-by-Process claims 44, 45 and 48 are being grouped

with the elected product claims since product-by-process claims are treated as product claims by the USPTO.

1. For applicant's convenience the following groups correspond to the newly presented claims: (GROUP I below is the elected invention):

Gp. 1, claim(s) 40-45 and 48, drawn to: fusion protein: SeCys peptide & surface protein.

Gp. 3, claim(s) 46-47, drawn to a library of SeCys terminal randomized peptides on the surface of an amplifiable genetic particle.

Gp. 6, claim(s) 49-53, drawn to a method of derivatizing SeCys in SeCys AND DERIVATIZED PEPTIDES containing peptides attached to surface genetic particles..

Gp. 8, claim(s) 54-58, drawn to an enzyme (substrate)-modified fusion (e.g. useful in method for selecting predetermined enzyme activity).

It is noted for the record, that the above compounds of Groups I (elected), III, VI and VIII are drawn to different fusion proteins containing different structure which possesses different chemical/biological properties; which are capable of separate manufacture and/or use and necessitate different and separately burdensome bibliographic/classification searches in patent and non-patent literature and addresses different issues under 35 USC 112/1,2 as well as prior art issues under 35 USC 102/103 since a reference to one invention would not be expected to anticipate or render obvious the other. Additionally, fusion proteins comprising selenocysteins and surface proteins "of an amplifiable genetic particle" OR "position on an amplifiable particle" (AS AMENDED) is not a common "special" technical feature since such fusion proteins were

known in the art (e.g. See references cited below including Larsen et al. US Pat. No. 5,272,078).

2. Claims 46-47 and 49-58 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

Priority

3. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 371 and 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994). As pointed out below, the presently claimed invention introduces is inadequately described and includes new matter. Accordingly, priority is denied for purposes of prior art.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 40-45 and 48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (NEW MATTER REJECTION).

In applicant's July 9, 2004 correspondence, applicant presented new claims which contained new limitations to which specification (or original claim support) was not indicated by applicant; nor was the Examiner able to locate specification support:

A. Claim 40 (and claims dependent thereon) : A fusion protein comprising a selenocysteine-containing peptide **covalently linked** to a surface protein **positioned on an** amplifiable particle.

There does not appear to be specific or representative support for the above bolded language. Changing "surface protein of an amplifiable particle" to the broader limitation --- surface protein positioned on an amplifiable particle – is not supported in the specification. The specification merely exemplifies phage surface display which is not representative of all amplifiable genetic particles or even polysome, virus, cell or spore claimed; since the specification fails to provide the necessary genetic constructs to provide support beyond the specific exemplified filamentous M13 phage.

B. Claim 42: "the selenocysteine is located at a predetermined, unique site".

C. Claim 43: "surface protein **comprises a native peptide bond**".

D. Claim 44: "A fusion .... Is expressed.. And a **part or all** of a selenocysteine insertion sequence".

E. Claim 45: "A fusion ... **is located adjacent to one or more nucleotides** from the TGA codon".

With regard to items B-E. both explicit and representative support has not been pointed to by applicant is it present in the specification. Even if such support were present for the fusion of a selenocysteine peptide to the M13 phage coat protein (e.g. g3p) such support is insufficient to support the currently claimed generic of fusion proteins (e.g. Secys peptide-"surface protein") positioned on "amplifiable particles".

6. Claims 40-45 and 48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (Lack of Written Description).

It is first noted that written description is legally distinct from enablement: "Although the two concepts of are entwined, they are distinct and each is evaluated under separate legal criteria. The written description requirement, a question of fact, ensures the that the inventor conveys to others that he or she had possession of the claimed invention; whereas, the enablement requirement, a question of law, ensures that the inventor conveys to others how to make and use the claimed invention." See 1242 OG 169 (January 30, 2001) citing *University of California v. Eli Lilly & Co*

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula [or] chemical name,of the claimed

subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.,* 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)]. As further stated by the Lilly court, the name if it does no more than distinguish the claimed genus from all others by function does not satisfy the written description requirement because it does not define any structural features commonly possessed by members of the genus that distinguish them from the others" See 43 USPQ2d at 1406.

The presently claimed invention broadly encompasses fusion proteins comprising:

a. a "selenocysteine containing peptide" covalently linked to

b. a "surface protein" positioned on an "amplifiable particle".

Accordingly, the peptide portion of the fusion protein has no fixed amino acid structure, length, conformation, function or source, but merely requires the presence of one (or more) selenocysteines.

Additionally, "surface protein" is not limited by amino acid structure, length, conformation, function or source.

Finally, the term "amplifiable particle" is not defined in the specification but merely enumerated to encompass phage, polysome, virus, cell or spore.

In support thereof the specification provides nucleic acid constructs for the fusion of a selenocysteine peptide to the M13 phage coat protein (e.g. g3p) which is not representative of:

a. all amplifiable genetic particles or even polysome, virus, cell or spore claimed;

b. any "surface protein" from whatever source (e.g. phage or non-phage); and

c. the requisite genetic constructs for a. and b.

Accordingly, applicant has failed to demonstrate possession of the open-ended genus of possible fusion protein and underlying genetic encoding constructs. In this regard, applicant is further referred to *University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997); "Guidelines for Examination of Patent Applications Under the 35 USC 112, first paragraph, 'Written Description' Requirement" published in 1242 OG 168-178 (January 30, 2001); and Univ. Of Rochester v G. D. Searle and Co. 249 F. Supp. 2d 216 (W.D.N.Y. 2003) affirmed by the CAFC on February 13, 2004 (03-1304) publication pending.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 40-45 and 48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. The term "surface protein **positioned on an amplifiable particle**" in claim 40 (and claims dependent thereon) is a relative term which renders the claim indefinite. The

term "positioned on an amplifiable particle" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree of positioning or means or determining location or position of a surface protein vis a vis an amplifiable particle, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. For example, for purposes of designing around, how does one known whether an expressed fusion protein is positioned (properly or improperly) on an "amplifiable particle".

b. In claim 40 and claims dependent thereon, the term "amplifiable particle" is indefinite. This term is not defined in the specification but merely exemplified (e.g. phage, polysome, virus, cell or spore). It is unclear what property/attribute/etc. distinguishes an "amplifiable particle" from a particle which is not amplifiable. The distinguishing features (if any) of an "amplifiable particle" are not readily apparent when considering the above-recited enumerated disparate Markush members (e.g. phage, polysome, virus, cell or spore). The term "amplify" can have many different definitions and may refer to a plethora of different properties e.g. to increase in size, number, strength etc.

c. The term "the selenocysteine **is located at a predetermined, unique site**" in claim 42 (and claims dependent thereon) is a relative term which renders the claim indefinite. The term "located at a predetermined, unique site" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree of uniqueness and/or means of measuring uniqueness or means of predetermining location, and one of ordinary skill in the art would not be reasonably apprised of the

scope of the invention. It is also noted that the claim is indefinite as to the nature of the predetermined, unique site. E.g. is the site nucleic acid or peptide or particle in nature?

d. In claim 43, the term "protein comprises a **native peptide bond**" is indefinite. It is unclear as to how one would distinguish a "native" peptide bond from a "non-native" peptide bond. In other words, given a fusion protein having a peptide bond; how does one classify the peptide bond as being "native" (and within the scope of the claim) as compared to a peptide bond that is "non-native" (and outside the scope of the claim) for purposes of infringing/designing around. The specification fails to define "native peptide bond(s)" nor provide a means (e.g. an assay or distinguishing chemical structure) for distinguishing native v. non-native peptide bonds.

e. The term "selenocysteine insertion sequence is located adjacent to one or more nucleotides from the TGA codon" in claim 45 is a relative term which renders the claim indefinite. The term "adjacent" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear as to how many nucleotides separate the insertion sequence from the one or more TGA codon to qualify as being adjacent. There is no specification/claim definition of the metes and bounds of the term "adjacent". In other words does a distance of 1, 2, 3, 5, 6, 8, 10 etc nucleotides away qualify as being "adjacent" for purposes of infringement and/or designing around?

f. The Markush listing in claim 48 is incomplete for failure to recite the category (e.g. compound, cell or otherwise) to which eubacteria, eukarya and archae are representative (e.g. group of ? consisting of .... Archae).

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 40-45 and 48 are rejected under 35 U.S.C. 102(a,b) as being anticipated by Sandman et al., JACS Vol. 122, pages 960-961 (Feb. 2000) .

The presently claimed invention (e.g. claim 40) broadly encompasses fusion proteins comprising:

a. a "selenocysteine containing peptide" covalently linked to

b. a "surface protein" positioned on an "amplifiable particle".

The reference discloses that selenopeptides can be recombinantly expressed as N-terminal fusions (e.g. covalently linked) to M13 phage (e.g. "an amplifiable particle") coat protein III (e.g. surface protein with "native peptide bond" and "positioned on "the amplifiable particle") "at a predetermined, unique site" anticipating claims 40-43. Claims 44, 45 and 48 are drawn to "product-by-process" limitations which is met by the reference product, which is within the presently claimed scope, regardless of means of manufacture. Alternatively, the reference appears to teach the process limitations e.g. the use of a TGA codon (encoding SeCis) "adjacent" to a SeCis insertion sequence (e.g. derived from a eubacteria, eukarya or archea). See entire document ; especially abstract ; figures and protocol.

12. Claims 40-45 and 48 are rejected under 35 U.S.C. 102(a,b) as being anticipated by Sandman et al., Nucleic Acid Res. Vol. 28(3) (2000) pages 755-761.

The presently claimed invention (e.g. claim 40) broadly encompasses fusion proteins comprising:

a. a "selenocysteine containing peptide" covalently linked to

b. a "surface protein" positioned on an "amplifiable particle".

The reference discloses that selenopeptides can be recombinantly expressed as N-terminal fusions (e.g. covalently linked) to M13 phage (e.g. "an amplifiable particle") coat protein III (e.g. surface protein with "native peptide bond" and "positioned on "the

amplifiable particle") "at a predetermined, unique site" anticipating claims 40-43. Claims 44, 45 and 48 are drawn to "product-by-process" limitations which is met by the reference product, which is within the presently claimed scope, regardless of means of manufacture. Alternatively, the reference appears to teach the process limitations e.g. the use of a TGA codon (encoding SeCis) "adjacent" to a SeCis insertion sequence (e.g. derived from a eubacteria, eukarya or archea). See entire document ; especially abstract ; figures and protocol.

13. Claims 40-45 and 48 are rejected under 35 U.S.C. 102(a,b,e) as being anticipated, or alternatively obvious under 35 U.S.C. 103, over Larsen et al. US Pat. No. 5,272,078 (12/93) alone, or if necessary further in view of Holliger et al. Structure, Vol. 5(2) (1997) pages 265-275 as evidence of inherency.

The presently claimed invention (e.g. claim 40) broadly encompasses fusion proteins comprising:

a. a "selenocysteine containing peptide" covalently linked to

b. a "surface protein" positioned on an "amplifiable particle".

The reference discloses that selenopeptides (e.g. 5'deiodinase variant mutants) can be recombinantly expressed in M13 phage (e.g. "an amplifiable particle") thus anticipating or alternatively rendering obvious the production of such mutants using M13 phage. See col. 15-16. Hollinger (e.g see abstract; page 266, left column; Figure 1)teach that M13 phage display the selenopeptides (e.g. library) fused to the N terminus of the M13 coat protein (e.g. gIII p) (e.g. surface protein with "native peptide bond" and "positioned

on "the amplifiable particle") "at a predetermined, unique site" anticipating claims 40-43. Claims 44, 45 and 48 are drawn to "product-by-process" limitations which is met by the Larsen reference product, which is within the presently claimed scope, regardless of means of manufacture. Alternatively, the Larsen reference appears to teach the process limitations e.g. the use of a TGA codon (encoding SeCis) "adjacent" to a SeCis insertion sequence (e.g. derived from a eubacteria, eukarya or archea). See entire document; especially abstract ; examples; figures and protocol (e.g. col. 9-14).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bennett Celsa whose telephone number is 571-272-0807. The examiner can normally be reached on 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bennett Celsa
Primary Examiner
Art Unit 1639

BC
February 11, 2005